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### The impact of the presence and extent of valve calcification on long-term results of percutaneous mitral commissurotomy

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**Purpose:** The indication of percutaneous mitral commissurotomy (PMC) is debated in patients (pts) with calcified mitral stenosis. We report outcome up to 20 years according to the presence and the extent of valve calcification.

**Methods:** PMC was performed in 1024 consecutive pts between 1986 and 1995: 710 pts had non-calcified valves (NCAL group) and 314 had valve calcification (CAL group) graded from 1 (mild) to 4 (extensive) using fluoroscopy. 177 pts (57%) were grade 1, 89 (28%) grade 2 and 48 (15%) grade 3 or 4.

**Results:** Good immediate results (GIR), defined as final valve area ≥1.5 cm² without mitral regurgitation >2/4, were obtained in 93% in NCAL group vs. 80% in CAL group (p<0.0001). Among CAL group, GIR were 87% for grade 1 calcification vs. 72% for grades 2,3 and 4 (p=0.01).

Good functional results (GFR) were defined as survival without intervention and in NYHA class I or II. 20-year rates of GFR were 38±3% for NCAL group and 12±3% in CAL group (p<0.0001). Among pts with GIR, 20 year rates of GFR were 40±3% in NCAL group vs. 21±3% in CAL group (p<0.0001). In CAL group predictors of GFR after GIR were: younger age (p=0.003), lower NYHA class (p=0.01), sinus rhythm (p=0.0002), lower post-PMC mean gradient (p<0.0001) and a lower extent of valve calcification (p=0.015).

According to the extent of valve calcification, 15-year rates of GFR after GIR were 35±4% for pts in grade 1 vs. 19±4% for pts in grades 2, 3 and 4 (p=0.01).

**Conclusion:** This study further confirms the negative prognostic impact of valve calcification on immediate and long-term results of PMC. PMC may, however, be considered to defer valve surgery in selected patients. In particular, more than 1 patient out of 3 with mild calcification still benefits from PMC 15 years after GIR. Young patients with few symptoms and in sinus rhythm are likely to benefit from PMC, even with calcified valves.

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### Left atrial remodeling after successful ballon mitral valvuloplasty

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**Background:** Left atrium (LA) remodeling has a crucial adverse impact on outcome and prognosis in mitral stenosis. Few studies have reported the effect of balloon mitral valvuloplasty (BMV) on LA volume and function. The aim of this study was to assess the evolution of LA volume and compliance 1 and 6 months after successful BMV in patients in sinus rhythm.

**Methods:** 95 consecutive patients (70% women; age 31±8 years; range 19-45) with severe mitral stenosis (mitral valve area ≤14 cm(2) ) who underwent successful BMV were included prospectively. Using-dimensional echocardiography, and according to the prolate ellipse method, LA volume, area and compliance (The maximum and the minimum LA volume were calculated from apical four- and two-chamber zoomed views of the LA, using the biplane method of discs. The difference between maximum and minimum LA volume divided by the minimum LA volume was used as an index of atrial compliance) were determined before BMV, and 1 month and 6 months after BMV. LV global systolic function was evaluated by EF, by the biplane Simpson method. Longitudinal left ventricular annular velocities were quantified by spectral pulsed wave Doppler tissue velocity imaging

**Results:** Mitral valve area increased from 0.88±0.2 to 1.8±0.26 cm(2) (P<0.0001). Mean mitral valve gradient (MVG) decreased from 14±6 to 6± 2 mmHg (P<0.0001) immediately after BMV. Indexed LA volume fell from 66±14 to 52±12 mL/m (2) (P=0.02) after BMV and to 45±13 mL/m (2) at 6 month (P<0.01) and an increase 0f the atrial index. Only patients with a median LA volume ≥55 mL/m (2) before BMV had a significant reduction in LA volume (P=0.0001). Decrease in LA volume was correlated with decreases in PA-RV peak diastolic gradient (r=0.45, P=0.008) and MVG (r=0.35, P=0.04).

**Conclusion:** In patients with mitral stenosis in sinus rhythm, successful BMV results in an immediate decrease in LA volume. This reduction, maximal immediately after BMV, correlates with decreases in MVG and PA-RV peak diastolic gradient, and is significant only when LA volume before BMV is severely enlarged.

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### Impact of percutaneous mitral valve commissurotomy on right ventricular function

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**Introduction:** The right ventricular function is an important determinant of clinical symptoms, exercise capacity, pre-operative survival and post-operative outcome in patients with mitral stenosis (MS).

**Objectif:** The aim of this work was to evaluate the impact of percutaneous mitral commissurotomy (PMC) on right ventricular function (RV) in patients with severe mitral stenosis managed in Center of cardiology- University Hospital IBN Rochd-Casablanca.

**Methods and results:** Of 150 patients there were 20 men and 130 women, their mean age was 35±10 years. One hundred were in New York Heart Association class II, 40 in class III and 10 in class IV. Eighty patients with atrial fibrillation.

Were studied before and after PMC. Multiple parameters of global and longitudinal RV function were assessed by conventional and tissue Doppler imaging echocardiography

Mitral surface area and hemodynamic parameters improved significantly after PMC; mean left atrial pressure fell from 18.76±6.18 to 10.65±4.38 mmHg (P<0.001), mean transmitral gradient from 14.03±4.70 to 4.63±2.05mmHg (p<0.001) and mitral valve area from 0.99±0.22 to 1.88±0.41 cm² (p<0.001), in the RV Tei index from 0.44+0.025 to 0.29+0.17 (P 1/4 0.021), in myocardial acceleration during isovolumic contraction (IVA) at the lateral tricuspid annulus from 0.36+0.11 m/s² to 0.25+0.07 m/s² (P 1/4 0.023), and in isovolumic contraction velocities at the lateral tricuspid annulus from 11.03+3.37 cm/s to 8.50+2.04 cm/s (P 1/4 0.034).

**Conclusion:** This study demonstrates that, in patients with MS, global right ventricular function improves in the majority of patients.

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### Increased Risk of Left Heart Valve Regurgitation Associated with Benfluorex Use in Patients with Diabetes Mellitus. A Multicentre Study

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**Background:** Benfluorex was withdrawn from European markets in June 2010 following reports of an association with heart valve lesions. The link

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between benfluorex and valve regurgitations was based on small observational studies and retrospective estimations. We therefore designed an echocardiography-based multicenter study to compare the frequency of left heart valve regurgitations in diabetic patients exposed to benfluorex for at least three months and in diabetic controls never exposed to the drug.

**Methods:** This reader-blinded controlled study conducted in ten centres in France included prospectively between November 2009 and September 2011 393 consecutive diabetic subjects previously exposed to benfluorex referred by primary care physicians for echocardiography screening and 393 diabetic controls. Using propensity scores, 303 patients and 303 controls were matched for age, gender, body mass index, smoking, dyslipidemia, hypertension, coronary artery disease, and previous use of other drugs associated with valve lesions. The main outcome measure was the frequency of mild or greater left heart valve regurgitations.

**Findings:** In the matched sample, the frequency and relative risk (OR) of mild or greater left heart valve regurgitations were significantly increased in benfluorex patients compared to controls: 30·0% vs. 13·5% (OR 2.96[1·94-4·53]) for aortic and/or mitral regurgitation; 21·1% vs. 5·0% (OR 5·63[3·08-10·3]) for aortic regurgitation, and 17·2% vs. 10·2% (OR 1·99[1·22-3·25]) for mitral regurgitation. The frequency of moderate left heart valve regurgitations was also increased among benfluorex patients vs. controls (7·3% vs. 0·7%; OR 13·9[3·21-60·7].

**Interpretation:** Our results indicate that use of benfluorex is associated with significant increase in the frequency of left heart valve regurgitations. The natural history of benfluorex-induced valve abnormalities needs further research.

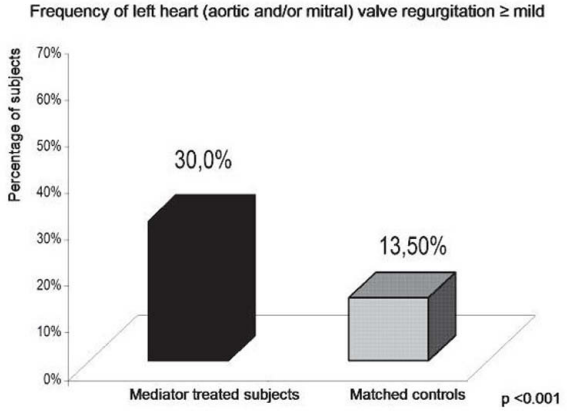


***Figure – Left heart regurgitations in patients vs. controls***

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**Standard deviation of the mean RR intervals measurement, a simple non invasive method to evaluate the prognosis of patients with myotonic dystrophy**

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Myotonic dystrophy (MD) is associated with a high risk of cardiac mortality. Several causes are implicated, bradycardia, atrial and ventricular arrhythmias, dilated cardiomyopathy and sudden death. Heart rate variability evaluation (HRV) is a non invasive method used to evaluate the prognosis of patients with heart disease. The purpose of the study was to evaluate the prognostic value of HRV determination for the stratification risk and the follow-up of patients with MD.

**Methods**: 156 patients, 79 men and 77 women, mean age 41±14 years, at the inclusion, were recruited for a MD. Patients were asymptomatic at the inclusion. The following studies were performed at the inclusion and repeated 4.5±3.5 years later in 124 of them. Recording of 24 hour Holter monitoring and measurement of HRV in the time domain was calculated every 5 minutes with the Elatec system; standard deviation of the mean RR intervals (SDNN) (ms) was determined. Left ventricular ejection fraction (LVEF) was evaluated at the same time by 2D echocardiography.

**Results**: LVEF decreased significantly from 62±8 to 58±11% (p< 0.03). None of them had sustained ventricular tachycardia. 19 patients died (12%) during the follow-up generally from cardiac and respiratory failure. Mean values of SDNN did not change significantly between first inclusion (126±42.5 ms) and last study (126±47 ms). At inclusion, SDNN was significantly shorter in patients who died than in alive patients (109±50 msec vs 128±41) (p <0.025). Among the patients who died, initial SDNN was missing in 6 patients, less than 100 msec in 10 patients and more than 100 msec in only 3 patients. Among total population only 40 patients had an initial SDNN <100 msec and 10 died (25%). Remaining patients had a SDNN >100 msec and only 3 patients died (3%)(p< 0.0001).

**Conclusions**: The modifications of HRV during the follow-up were not useful for the prediction of the occurrence of dilated cardiomyopathy or of life-threatening arrhythmias in myotonic dystrophy, although LVEF decreased with time. However, a low HRV (< 100msec) at the first evaluation was predictive of increasing mortality from 3 to 25%.

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**Clinical and echographic characteristics of patients exposed to fenfluramin derivatives:**
**Results of a prospective, monocenter observational study**

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**Objectives:** Fenfluramine derivatives have been associated with significant risk of developing cardiac valvulopathy. This prospective study evaluated characteristics of patients hospitalized in cardiology and who have been exposed to these drugs.

**Methods:** Between july 2011 and february 2012, patients admitted in the cardiology department, University Center of Montpellier, France, were questioned about past exposition to fenfluramine derivatives. In case of positive response, a questionnaire assessing prescribing patterns and previous medical history was proposed and echocardiography was performed. All usual echocardiographic parameters were analysed. We applied criteria from the French multicenter registry for diagnosis of drug-induced valvulopathy.

**Results:** Ninety patients exposed to the drugs were included. Sixty-seven percent were women (n=60). Fifty-three percent had diabete (n=47). Ninety percent were exposed to benfluorex (n=81). Mean treatment duration was 48 months (IC95%; 36,5-60,2). Valvular regurgitations were observed in 62,2% of patients (n=51) while 19% of patients (n=15) had pulmonary hypertension. Distribution of valvulopathies is summarized in table 1. Highly probable induced valvulopathies were mild to moderate in all except 3 cases.

**Conclusion:** In absence of definite knowledge about evolution of drug-induced valve disease, systematic questioning concerning fenfluramine derivatives use could be recommended in hospitalized patients.

***Table 1 – Distribution of regurgitations***

| | Patients | Mitral R | Aortic R |
|---|---|---|---|
| HP | 16 (20,3%) | 8 (10,7%) | 11 (14,3%) |
| PI | 28 (34,1%) | 20 (24,4%) | 13(16,0%) |
| UI | 22 (26,8%) | 15 (18,3%) | 11 (13,4%) |

*(HP: highly probable induced regurgitations; PI: possibly induced regurgitations; UI: unlikely induced regurgitations; R: regurgitation)*